REMARKS

This Response is submitted in reply to the non-final Office Action mailed on November 9, 2010. A Petition for a one month extension of time is submitted herewith. The Commissioner is hereby authorized to charge $130.00 for the Petition for a one month extension of time and any additional fees that may be required or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-00702 on the account statement.

Claims 1-14 and 22-25 are pending in the application. Claims 15-21 were previously withdrawn from consideration. In the Office Action, Claims 1-14 and 22-25 are rejected under 35 U.S.C. §103. Applicants respectfully traverse the rejections for at least the reasons set forth below.

In the Office Action, Claims 1-3, 5, 6, 8, 10-14 and 22-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over WO 01/22837 to Kuslys et al. ("*Kuslys*") in view of EP 0904784 to Van Hoey-de-Boer et al. ("*Van Hoey-de-Boer*") and U.S. Publication No. 2003/0060445 to Wilson ("*Wilson*"). Applicants respectfully traverse the rejections for at least the reasons set forth below.

Independent Claim 1 to recites, in part, an infant or follow-on formula comprising a source of proteins, a source of lipids, a source of carbohydrates, a probiotic and a calcium/phosphorus weight ratio ranging between 1.4 and 3. In an embodiment, the claimed infant or follow-on formula provides a unique combination of protective nutrients ensuring growth and metabolic patterns similar to those of breastfed infants, with the intention of enabling similar health characteristics to be enjoyed in later childhood and adulthood. The claimed infant or follow-on formula presents a reduced load on immature organs and favors the natural growth of Bifidobacteria and other beneficial microflora in the large intestine of breastfed infants.

Applicants respectfully submit that the skilled artisan would have no reason to combine *Kuslys*, *Van Hoey-de-Boer,* and *Wilson* to arrive at the present claims because the cited references are directed to unrelated products that have completely different objectives. For example, *Kuslys* is entirely directed to a composition having casein and whey protein that may be used as a replacement for human milk, while maintaining a similar protein concentration. See, *Kuslys*, page 2, lines 1-11. *Van Hoey-de-Boer* is entirely directed to a nutritional preparation for

use in treating disorders of the gastrointestinal tract without the need of determining before hand which microorganism is responsible for the disorder. *Van Hoey-de-Boer* provides a list of potentially helpful bacteria and optimum conditions for the growth of same. See, *Van Hoey-de-Boer,* columns 1-2, paragraphs 7-11. *Wilson* is entirely directed to the use of a composition having a synergistic prebiotic comprising oligofructose and sialyllactose. The composition may be used to inhibit the binding of pathogenic microorganisms to human tissue. See, *Wilson*, Abstract; page 1, paragraph 10. As such, the cited references are directed to entirely distinguishable compositions that are used for entirely distinguishable purposes.

Further, Applicants submit that what the Patent Office has done is to rely on hindsight reconstruction of the claimed invention. Applicants respectfully submit that it is only with a hindsight reconstruction of Applicants' claimed invention that the Patent Office is able to even attempt to piece together the teachings of the prior art so that the claimed invention is allegedly rendered obvious. Instead, the claims must be viewed as a whole as defined by the claimed invention and not dissected into discrete elements to be analyzed in isolation. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983); *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). One should not use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d at 1075. (Fed. Cir. 1988).

Moreover, Applicants also respectfully submit that if it is proper for the Patent Office to combine any number of references to arrive at the present claims simply because each reference suggests an element of the present claims, then every invention would effectively be rendered obvious. Instead, the skilled artisan must have a reason to combine the cited references to arrive at the present claims. Applicant respectfully submits that such a reason is not present in the instant case.

Applicants also submit that, even if the Patent Office has made a *prima facie* case of obviousness, Applicants have rebutted the *prima facie* case of obviousness by demonstrating surprising and unexpected results. Applicants submit herewith a Declaration under 37 C.F.R. §1.132 ("*Declaration*" attached hereto as Exhibit A) that demonstrates the deficiencies of the prior art with respect to the present claims. Specifically, the *Declaration* demonstrates that Applicants have surprisingly found that compositions of the present claims provide a unique

combination of protective nutrients with a view to ensuring growth and metabolic patterns similar to those of breast-fed infants. The present claims aim at achieving such a result by adapting the formula in such a way that the physiological effect of consuming the improved formula is closer to the physiological effect of consuming breast milk. As supported by the *Declaration*, Applicants have found that the combination of a protein source containing modified sweet whey protein ("MSW") in an amount of at least 40% of the proteins and a probiotic leads to certain unexpected and surprising beneficial effects.

It has long been known that during the months prior to weaning differences in the microflora composition between breast-fed and formula-fed infants are apparent. In full-term infants, breast feeding induces the development of a microflora rich in *Bifidobacterium sp.* Other anaerobes such as *Clostridium sp.* and *Bacteriodes sp.* are more rarely isolated, and facultative anaerobes such as *Escherichia sp.* and *Enterococci* are even less numerous. In contrast to breast-fed infants, formula-fed infants are often colonized by a more diverse microbiota including *Clostridium perfringens*, *Escherichia coli* and *Bacteroides* in addition to Bifidobacteria. These differences in the microflora may partly explain the lower incidence of intestinal infection observed in breast-fed infants compared with formula-fed infants.

As discussed in the *Declaration*, Applicants have surprisingly discovered unexpected and synergistic effects between the protein source in the formulas of the present claims and the probiotic, such that a microflora similar to that found in breast-fed infants is rapidly established and maintained in infants fed a formula according to the present claims. This has now been demonstrated clinically, as is discussed in the *Declaration*. For example, attached to the *Declaration* are the following documents: i) the poster presented at the 2005 meeting of NASPGHAN; and ii) the Abstract submitted to PAS 2008.

The poster presented at the 2005 meeting of NASPGHAN illustrates the fecal Bifidobacteria counts of infants fed breast milk compared to those of infants fed a formula described as NAN, which is an infant formula produced by an affiliate of Applicants. The NAN formula has a protein source that is 60% MSW. As illustrated, it can be seen that the amounts of Bifidobacteria in the stools of the formula fed to infants was comparable to that for the breast fed infants.

The Abstract submitted to PAS 2008 describes the results of a separate clinical trial in which the fecal counts of infants fed a conventional infant formula (i.e., without MSW) is compared to that of infants fed the NAN formula, and with that of infants fed the NAN formula supplemented with a strain of *Bifidobacterium longum*. It is shown that the amount of *Bifidobacteria* in the stools of the infants fed the NAN formulas was significantly higher than the conventional formula. The study has established that an even better result was obtained with the formula containing MSW and *B. longum* as regards the important criterion of colonization with *Clostridia sp.* Specifically, analysis of the stools showed that 97% of the infants fed the conventional formula were colonized with *Clostridia* compared with 93% of those fed unsupplemented NAN and only 86% of those fed NAN supplemented with *B. longum*. This is a significant reduction in the level of colonization with *Clostridia sp.* which, as noted above, as regarded as undesirable constituents of the infant intestinal microflora.

The effects of administering the NAN compositions to infants as compared to the NAN formulations with probiotics are further detailed in Exhibit 3 of the *Declaration*. The publication of Exhibit 3 describes a prospective, controlled, double-blind, randomized trial performed on infants healthy, full-term infants that were exclusively fed a control formula or study formulas containing certain bacteria. The control formula of the trial was the unsupplemented formula known as NAN, as described above. The study formula groups included various combinations of probiotics and synbiotics. The objective of the trial was to evaluate infant formulas containing probiotics and synbiotics for safety and tolerance. Safety and tolerance were assessed based on weight gain during the treatment period (primary outcome), as well as recumbent length, head circumference, digestive tolerance, and adverse events (secondary outcomes), which were evaluated at 2, 4, 8, 12, 16 and 52 weeks of age.

As detailed in the *Declaration*, two hundred eighty-four infants were enrolled in the randomized trial of Exhibit 3. During the treatment period, difference in mean weight gain between control and study formula groups in both the intention-to-treat and per protocol populations were within the predefined equivalence boundaries of ±3.9 g/d, indicating equivalent weight gain. Secondary outcomes did not show significant differences between groups during the treatment period. Interestingly, however, whereas during the treatment period there were no differences in the frequency of symptoms of gastrointestinal intolerance, diarrhea, and other

adverse events between infants of any of the study formula groups and those in the control formula group, at the 1-year follow-up, infants in the group that received the formulas containing probiotics has significantly few incidents of diarrhea. Surprisingly, the decrease in the incidence of diarrhea was observed several months after infants had stopped taking the probiotic-supplemented formula.

As is further supported by the *Declaration* and discussed in the specification, the compositions of the present claims provide many unexpected nutritional benefits. For example, as discussed in the specification, the present compositions provide for a better protein utilization, a plasma amino acid pattern close to that of breast-fed infants, and adequate growth rates. The improved amino acid profile of the present compositions results in better protein utilization, as is shown by the higher percentage of nitrogen retention found in infants fed with a formula according to the present claims as compared with infants fed a regular whey-adapted formula. This is clearly illustrated by Table 5 in the specification.

The compositions of the present claims, as supported by the *Declaration*, further provide a protein content that meets the needs of normal term infants during the first months of life without excessive energy intake or increase body mass index, present a reduced load on immature organs of infants, and improve stool consistency and reduce the frequency of hard stools.

In contrast, as supported by the *Declaration*, Applicants respectfully submit that the cited references fail to disclose or suggest the above-identified benefits of the combination of the MSW and probiotics. Accordingly, Applicants respectfully request that the obviousness rejections in view of *Kuslys*, *Van Hoey-de-Boer* and *Wilson* be reconsidered and the rejections be withdrawn.

In the Office Action, Claims 4 and 7 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Kuslys* in view of *Van Hoey-de-Boer* and *Wilson*, further in view of the publication to Holm ("*Holm*") and the publication to Ishibashi et al. ("*Ishibashi*"). Claim 9 is rejected under 35 U.S.C. §103(a) as being unpatentable over *Kuslys* in view of *Van Hoey-de-Boer* and *Wilson*, further in view of EP 1048226 to Kratky et al. ("*Kratky*"). Applicants respectfully submit that the patentability of Claim 1 as previously discussed renders moot the obviousness rejection of Claims 4, 7 and 9 that depend from Claim 1. In this regard, the cited art

fails to teach or suggest the elements of Claims 4, 7 and 9 in combination with the novel elements of Claim 1.

In the Office Action, Claims 1-3, 5-6, 9-14 and 22-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Kratky* in view of *Van Hoey-de-Boer* and *Wilson*. Applicants respectfully traverse the rejections for at least the reasons set forth below.

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contrast to breast-fed infants, formula-fed infants are often colonized by a more diverse microbiota including *Clostridium perfringens*, *Escherichia coli* and *Bacteroides* in addition to Bifidobacteria. These differences in the microflora may partly explain the lower incidence of intestinal infection observed in breast-fed infants compared with formula-fed infants.

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As detailed in the *Declaration*, two hundred eighty-four infants were enrolled in the randomized trial of Exhibit 3. During the treatment period, difference in mean weight gain between control and study formula groups in both the intention-to-treat and per protocol populations were within the predefined equivalence boundaries of ±3.9 g/d, indicating equivalent weight gain. Secondary outcomes did not show significant differences between groups during the treatment period. Interestingly, however, whereas during the treatment period there were no differences in the frequency of symptoms of gastrointestinal intolerance, diarrhea, and other adverse events between infants of any of the study formula groups and those in the control formula group, at the 1-year follow-up, infants in the group that received the formulas containing probiotics has significantly few incidents of diarrhea. Surprisingly, the decrease in the incidence of diarrhea was observed several months after infants had stopped taking the probiotic-supplemented formula.

As is further supported by the *Declaration* and discussed in the specification, the compositions of the present claims provide many unexpected nutritional benefits. For example, as discussed in the specification, the present compositions provide for a better protein utilization, a plasma amino acid pattern close to that of breast-fed infants, and adequate growth rates. The improved amino acid profile of the present compositions results in better protein utilization, as is shown by the higher percentage of nitrogen retention found in infants fed with a formula

according to the present claims as compared with infants fed a regular whey-adapted formula. This is clearly illustrated by Table 5 in the specification.

The compositions of the present claims, as supported by the *Declaration*, further provide a protein content that meets the needs of normal term infants during the first months of life without excessive energy intake or increase body mass index, present a reduced load on immature organs of infants, and improve stool consistency and reduce the frequency of hard stools.

In contrast, as supported by the *Declaration*, Applicants respectfully submit that the cited references fail to disclose or suggest the above-identified benefits of the combination of the MSW and probiotics. Accordingly, Applicants respectfully request that the obviousness rejections in view of *Kratky*, *Van Hoey-de-Boer* and *Wilson* be reconsidered and the rejections be withdrawn.

In the Office Action, Claims 4 and 7 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Kratky* in view of *Van Hoey-de-Boer* and *Wilson,* further in view of the combination of *Holm* and *Ishibashi.* Applicants respectfully submit that the patentability of Claim 1 as previously discussed renders moot the obviousness rejection of Claims 4, 7 and 9 that depend from Claim 1. In this regard, the cited art fails to teach or suggest the elements of Claims 4, 7 and 9 in combination with the novel elements of Claim 1.

In the Office Action, Claims 1-7, 10-14 and 22-25 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1, 6-13 and 20 of copending Application 10/564,805 ("the '805 application"). Claim 8 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1, 6-13 and 20 of the '805 application further in view of *Wilson* and *Kuslys*. Claim 9 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1, 6-13 and 20 of the '805 application further in view of *Wilson* and *Kratky*. For purposes of advancing the prosecution of this application, Applicants have elected to overcome such rejection through the enclosed Terminal Disclaimer. Such election shall not be deemed an admission as to the propriety or accuracy of the Patent Office's conclusions or rejections.

Accordingly, Applicants respectfully request that the provisional rejection of Claims 1-14 and 22-25 under the nonstatutory obviousness-type double patenting be reconsidered and withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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EXHIBIT A